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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/665,430	09/22/2003	Paul D. Rubin	4821-523	6519

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WASHINGTON, DC 20001-2113

EXAMINER

TRAN, SUSAN T

ART UNIT	PAPER NUMBER
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1615

DATE MAILED: 03/30/2006

Please find below and/or attached an Office communication concerning this application or proceeding.

**Office Action Summary**

Application No.

10/665,430

Applicant(s)

RUBIN ET AL.

Examiner

Susan T. Tran

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-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

**Period for Reply**

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

**Status**

- 1) ☒ Responsive to communication(s) filed on 18 January 2006.
- 2a) ☒ This action is **FINAL**. 2b) ☐ This action is non-final.
- 3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

**Disposition of Claims**

- 4) ☒ Claim(s) 21 and 23-34 is/are pending in the application.
- 4a) Of the above claim(s) 29-34 is/are withdrawn from consideration.
- 5) ☐ Claim(s) \_\_\_\_\_ is/are allowed.
- 6) ☒ Claim(s) 21 and 23-28 is/are rejected.
- 7) ☐ Claim(s) \_\_\_\_\_ is/are objected to.
- 8) ☐ Claim(s) \_\_\_\_\_ are subject to restriction and/or election requirement.

**Application Papers**

- 9) ☐ The specification is objected to by the Examiner.
- 10) ☐ The drawing(s) filed on \_\_\_\_\_ is/are: a) ☐ accepted or b) ☐ objected to by the Examiner.  
Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).  
Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).
- 11) ☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

**Priority under 35 U.S.C. § 119**

- 12) ☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).
- a) ☐ All b) ☐ Some \* c) ☐ None of:
- ☐ Certified copies of the priority documents have been received.
  - ☐ Certified copies of the priority documents have been received in Application No. \_\_\_\_\_.
  - ☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

\* See the attached detailed Office action for a list of the certified copies not received.

**Attachment(s)**

- |  |   |
|--|---|
| 1) <input type="checkbox"/> Notice of References Cited (PTO-892)   | 4) <input type="checkbox"/> Interview Summary (PTO-413)<br>Paper No(s)/Mail Date. _____ |
| 2) <input type="checkbox"/> Notice of Draftsperson's Patent Drawing Review (PTO-948)                                   | 5) <input type="checkbox"/> Notice of Informal Patent Application (PTO-152)             |
| 3) <input type="checkbox"/> Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08)<br>Paper No(s)/Mail Date _____ | 6) <input type="checkbox"/> Other: _____  |

## DETAILED ACTION

### *Election/Restrictions*

Claims 29-34 are withdrawn from further consideration pursuant to 37 CFR 1.142(b) as being drawn to a nonelected species, there being no allowable generic or linking claim. Election was made **without** traverse in the reply filed on 01/18/06.

### ***Claim Rejections - 35 USC § 103***

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

(a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negated by the manner in which the invention was made.

The factual inquiries set forth in *Graham v. John Deere Co.*, 383 U.S. 1, 148 USPQ 459 (1966), that are applied for establishing a background for determining obviousness under 35 U.S.C. 103(a) are summarized as follows:

1. Determining the scope and contents of the prior art.
2. Ascertaining the differences between the prior art and the claims at issue.
3. Resolving the level of ordinary skill in the pertinent art.
4. Considering objective evidence present in the application indicating obviousness or nonobviousness.

Claims 21 and 23-28 are rejected under 35 U.S.C. 103(a) as being unpatentable over Johnson WO 92/00103, in view of Young US 5,712,302.

Johnson teaches a pharmaceutical composition comprising combination of a 5-HT<sub>3</sub> receptor antagonist, a 5-HT reuptake inhibitor, and a pharmaceutical acceptable carrier (page 1, lines 15-19; page 2, lines 31 through page 3, lines 1-9; and claims 1&2).

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Johnson further teaches 5-HT<sub>3</sub> receptor antagonist includes ondansetron, and 5-HT reuptake inhibitor includes fluoxetine (page 1, line 32; page 2, lines 6-10; claim 7). The composition can be administered orally or parenterally (page 4, lines 14-24).

Johnson does not expressly teach the 5-HT<sub>3</sub> receptor antagonist comprises the claimed ondansetron.

Young teaches ondansetron is a safe and competitive antagonist 5-HT<sub>3</sub> receptor antagonist (column 2, lines 60-67). Young further teaches the use of optically pure R(+) ondansetron or salt thereof, substantially free of its S(-) stereoisomer for the treatment of diseases, while decreasing the usual adverse effects (column 5, lines 61-67). Young also teaches a composition comprising optically pure R(+) ondansetron or salt thereof, substantially free of its S(-) stereoisomer (see abstract and claim 1). Salt thereof, includes hydrochloride (column 9, lines 24-34, and claim 2). Optically pure R(+) ondansetron contains at least 99% by weight of R(+) ondansetron, and 1% or less of S(-) ondansetron (column 7, lines 48-58). The amount of R(+) ondansetron ranges from 0.001 mg to 35 mg (column 8, lines 52-54). The composition further comprises pharmaceutically acceptable carrier, and other therapeutic agents (column 9, lines 16-24; and column 10, lines 7-24). Young further teaches the composition is suitable for oral or parenteral administration (column 9, lines 9-15). Thus, it would have been obvious to one of ordinary skill in the art to modify the 5-HT<sub>3</sub> receptor antagonist of Johnson using the optically pure R(+) ondansetron or salt thereof, substantially free of its S(-) stereoisomer in view of the teaching of Young, because Young teaches the use of optically pure R(+) ondansetron or salt thereof, substantially free of its S(-)

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stereoisomer for the treatment of behavioral disorders including depression, intense sadness or agitation, while decreasing the usual adverse effects (column 5, lines 61-67; and column 6, lines 1-5), and because Johnson teaches the combination of 5-HT<sub>3</sub> receptor antagonist and 5-HT reuptake inhibitor for the treatment of depression and/or migraine (page 2, lines 19-20; and page 6, lines 33-36).

### ***Response to Arguments***

Applicant's arguments filed 01/18/06 have been fully considered but they are not persuasive.

While applicant admits that Johnson teaches ondansetron and fluoxetine (see Remarks at page 5, 2<sup>nd</sup> paragraph), applicant argues that those of ordinary skill in the art would not have been motivated to specifically select these two agents and use them in a combination, because the combination of ondansetron and fluoxetine is merely one of numerous possible combinations disclosed in Johnson application. Applicant further argues that Johnson at page 1, lines 24-27, teaches four different combinations of three classes of molecules. However, applicant's attention is called to claim 2 of Johnson publication, where Johnson teaches a specific combination of 5-HT<sub>3</sub> antagonist (ondansetron) and 5-HT reuptake inhibitor (fluoxetine). Accordingly, there is a specific guidance to motivate the skilled artisan to combine these two agents.

Applicant argues that Johnson discloses numerous species for 5-HT reuptake inhibitor. However, it is noted that claim 7 of Johnson discloses a small Markush Group of only 12 5-HT reuptake inhibitor that includes fluoxetine. Therefore, it is not

unreasonable to envision selecting/using fluoxetine. A genus may be so small that, when considered in light of the totality of the circumstances, it would anticipate the claimed species or subgenus. For example, it has been held that a prior art genus containing only 20 compounds and a limited number of variations in the generic chemical formula inherently anticipated a claimed species within the genus because "one skilled in [the] art would... envisage each member " of the genus. *In re Petering*, 301 F.2d 676, 681, 133 USPQ 275, 280 (CCPA 1962). Accordingly, it would have been obvious to one of ordinary skill in the art to select fluoxetine from claim 7 to combine with ondansetron in view of the disclosure of claim 2.

Applicant argues that Young does not teach or suggest anything regarding the desirability of the specific combination of R(+) ondansetron and fluoxetine. In response to applicant's argument, the test for obviousness is not whether the features of a secondary reference may be bodily incorporated into the structure of the primary reference; nor is it that the claimed invention must be expressly suggested in any one or all of the references. Rather, the test is what the combined teachings of the references would have suggested to those of ordinary skill in the art. See *In re Keller*, 642 F.2d 413, 208 USPQ 871 (CCPA 1981). The examiner recognizes that obviousness can only be established by combining or modifying the teachings of the prior art to produce the claimed invention where there is some teaching, suggestion, or motivation to do so found either in the references themselves or in the knowledge generally available to one of ordinary skill in the art. See *In re Fine*, 837 F.2d 1071, 5 USPQ2d 1596 (Fed. Cir. 1988) and *In re Jones*, 958 F.2d 347, 21 USPQ2d 1941 (Fed. Cir. 1992). In this case,

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Young is cited for the suggestion to use R(+) ondansetron to obtain clearer dose definitions of efficacy vis a vis adverse effects (column 6, lines 1-29).

### ***Conclusion***

**THIS ACTION IS MADE FINAL.** Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the mailing date of this final action.

### ***Correspondence***

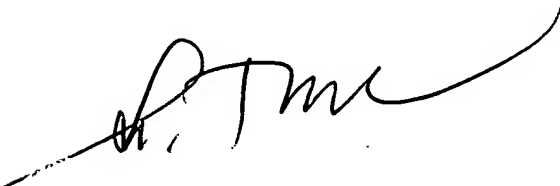
Any inquiry concerning this communication or earlier communications from the examiner should be directed to Susan T. Tran whose telephone number is (571) 272-0606. The examiner can normally be reached on Monday through Thursday 6:00 am to 4:30 pm.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Thurman K. Page can be reached on (571) 272-0602. The fax phone

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number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see <http://pair-direct.uspto.gov>. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).



S. Tran  
Examiner  
Art Unit 1615